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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,752	04/08/2005	Shuh Narumiya	Q87373	7330

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EXAMINER	
LEWIS, AMY A	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,752	NARUMIYA, SHUH	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,11-13,15 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,11-13,15 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 3/30/2007, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/30/2007 has been entered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 9, 11-13, and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Sheller et al. ("The prostaglandin E agonist, misoprostol, inhibits airway IL-5 production in atopic asthmatics," *Prostaglandins & Other Lipid Mediators* 70 (Sept. 2002) 185-193).

Sheller et al. teach that misoprostol is a stable, orally active prostaglandin E agonist effective in treating atopic asthma via signaling through the EP3 receptor (see: title, abstract, and Discussion at page 190). The reference also teaches oral administration at doses of 400μg and 600μg (every 6 hours) (see; p. 186, Introduction).

2) Claims 9, 11-13, 15, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,252,602 (to Alam et al.).

Alam et al. teach methods for treating late-phase allergic reactions with misoprostol (abstract). The late-phase allergic reactions can include the following: asthma, allergic rhinitis, contact dermatitis, anaphylaxis, urticaria, cutaneous allergic response (see: claims 2, 14, 21; col. 1, lines 5-15). The reference teaches various dosages ranging from 200μg to 5mg, 100μg to 400μg, 25 μg to 800 μg, (see claims 7-12). The reference teaches parenteral, oral, topical, intranasal, or aerosol administration (see col. 4 lines 65+). The reference also teaches that misoprostol is a PGE analogue with similar immunomodulatory effects as it's parent compound prostaglandin E (see col. 2, lines 3-18). The reference also teaches co-administration with nonsteroidal anti-inflammatory drugs (col. 2, lines 15-16).

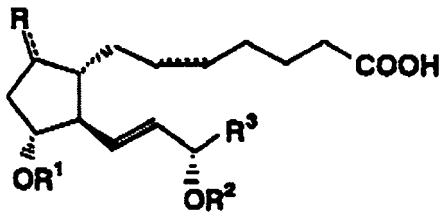
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3) Claims 15, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1008588 (Ono Pharmaceutical Co., Inc.), in view of Sheller et al. ("The prostaglandin E agonist, misoprostol, inhibits airway IL-5 production in atopic asthmatics," *Prostaglandins & Other Lipid Mediators* 70 (Sept. 2002) 185-193). This rejection is maintained over claims 9, 11-13, and 15, and newly applied to claims 18-19.

The '588 reference discloses a compound and pharmaceutical composition comprising a compound having the following general structure:



(I)

The '588 reference teaches these compounds are prostaglandin E derivatives and bind the EP2 and EP3 prostaglandin subtype receptor (see: paragraphs [0002-0004] on page 2 and [0035] on page 11). The '588 reference also teaches (see instant claim 15; the presently elected species compound I-1) of 11α,15α-dimethoxy-9-oxoprosta-5Z,13E-dienoic acid as a preferred compound of formula (I) (see page 3). The reference also teaches a dose of 1 μg to 100mg by oral administration and 0.1μg to 10mg by parenteral (intravenous) administration (see [0037] page 11).

The '588 reference does not teach that EP3 agonists are effective in treating allergies such as asthma.

Sheller et al. teach that misoprostol is a stable, orally active prostaglandin E agonist effective in treating atopic asthma via signaling through the EP3 receptor (see: title, abstract, and

Discussion at page 190). The reference also teaches oral administration at doses of 400μg and 600μg (every 6 hours) (see; p. 186, Introduction).

Having been taught by Sheller et al. that prostaglandin E agonists, particularly those which act on the E3 receptor are useful in the treatment of atopic asthma, and by the '588 reference that the prostaglandin E derivative, 11α,15α-dimethoxy-9-oxoprosta-5Z,13E-dienoic acid in particular, agonizes the E3 receptor, one of ordinary skill in the art would have been motivated to use 11α,15α-dimethoxy-9-oxoprosta-5Z,13E-dienoic acid in the treatment of atopic asthma. One of ordinary skill in the art would have had a reasonable expectation of success is such treatment, having been taught by Sheller et al. that such specific prostaglandin E derivatives are useful in the treatment of atopic asthma. Further, one of ordinary skill in the art would have been motivated to combine the '588 reference and Sheller et al. because both are directed to agonizing EP3 and the inhibition of prostaglandin E2. Moreover, the selection of a known material based on its suitability for its intended use can support a *prima facie* obviousness determination and herein the teachings of Sheller et al. that agonizing PGE2 receptors such as EP3, results in a reduction of IL-5 and evidently eosinophils, mast cells and/or T lymphocyte production (all inflammatory cells), in light of the teaching in the '588 reference that EP3 is a recognized receptor for PGE2 supports a case of *prima facie* obviousness.

4) Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1008588 (Ono Pharmaceutical Co., Inc.), in view of Sheller et al. ("The prostaglandin E agonist, misoprostol, inhibits airway IL-5 production in atopic asthmatics," *Prostaglandins & Other Lipid Mediators* 70 (2002) 185-193), and further in view of U.S. Patent No. 5,485,827.

The '588 reference and Sheller et al. are applied as above. The references do no teach combination therapy with other agents.

U.S. Patent No. 5,485,827 provides a general teaching of drugs used in the treatment of asthma (see: col. 1 lines 40-55):

> Drugs used to treat asthma fall generally into two categories: those which act mainly as inhibitors of inflammation, such as corticosteroids and cromolyn sodium, and those which act primarily as relaxants of the tracheobronchial smooth muscle, such as theophylline and its derivatives, beta-adrenergic agonists, and anticholinergics. Some of these bronchodilators may be administered orally, while others are generally given by intravenous or subcutaneous injection or by inhalation of the drug in an appropriate form, such as aerosolized powder (i.e., delivered in the form of a finely divided solid, suspended in a gas such as air), or aerosolized droplets (delivered in the form of a fine mist). Asthma patients typically self-administer bronchodilator drugs by means of a portable metered-dose inhaler, employed as needed to quell or prevent intermittent asthma attacks.

Combining agents which are known to be useful for allergies individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. Since it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining the claimed active and anti-asthma drugs flows logically from their having been individually taught in the prior art. Thus, the combined references teach and make *prima facie* obvious how to use the claimed invention at the time that it was made.

Response to Arguments:

Applicant's arguments filed 17 July 2006 have been fully considered but they are not persuasive. Applicant's argue that the Sheller et al. reference does not teach that an EP3 agonist can be used to treat an allergic disease. To the contrary, Sheller et al. teaches administration of misoprostol to patients with atopic asthma; as the method taught by Sheller et al. is the same as

that claimed by applicant, the reference does in fact teach the instantly claimed method of treatment using a compound of formula (I), which includes misoprostol to treat atopic asthma. That Sheller et al. may not have unraveled the mechanism of action of the active agent does not detract from its use as art since it teaches the limitations of the claims.

In response to Applicant's arguments regarding misoprostol and the reduction of IL-5 in reduction of allergic response, and it's effect on the EP3 receptor, such limitations are not included in the instant claims. Further, even if the limitations were present, "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." MPEP § 2112 citing *Atlas Powder Co. v. Ireco Inc.* 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed Cir. 1999). The explanation or observation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the desired therapeutic effect. This, the assessment of patentability under 35 U.S.C. §§ 102 and 103 is based upon the therapeutic applications and effects, not the mechanism by which they exert that therapeutic effect.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is 571-272-9032. The examiner can normally be reached on Monday-Friday 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy A. Lewis

Ardin H. Marschel 9/28/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER